

CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY
DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH
SUMMARY OF TOXICOLOGY DATA

3-Iodo-2-Propynyl Butyl Carbamate

Chemical Code # 001938, DPN # 50237
SB 950 # 479

July 25, 1996
Revised: 9/4/02; 10/23/03, 12/1/04

I. DATA GAP STATUS

Combined, rat:	No data gap, possible adverse effect
Subchronic, rat (oral):	No data gap, possible adverse effect
(dermal):	No data gap, possible adverse effect
Chronic toxicity, dog:	Data gap, no study on file
Oncogenicity, mouse:	No data gap, no adverse effect
Reproduction, rat:	Data gap, inadequate study, no adverse effect indicated
Teratology, rat:	Data gap, inadequate study, possible adverse effect indicated
Teratology, rabbit:	No data gap, no adverse effect
Gene mutation:	No data gap, no adverse effect
Chromosome effects:	No data gap, no adverse effect
DNA damage:	Data gap, inadequate study, no adverse effect
Neurotoxicity, rat:	No data gap, no adverse effect

Toxicology one-liners are attached.

All record numbers through 211915 were examined.

** indicates an acceptable study.

Bold face indicates a possible adverse effect.

File name: T031008

Prepared by Green & Silva, 9/4/02; Silva, 10/23/03 & 12/1/04

IPBC is an antimicrobial pesticide for non-food uses.

US EPA Reregistration Eligibility Document (RED) was published March, 1997.

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

These pages contain summaries only. Individual worksheets may contain additional effects.

COMBINED, RAT

**** 029, 030 114800, 114801,** "3-Iodo-2-Propynyl Butyl Carbamate (IPBC) 104 Week Dietary Carcinogenicity Study in Rats", (Inveresk Research International, Musselburgh, Scotland, Everett, D.J., Perry, C.J., Hudson, P., Finn, J.P.; Report #: 5261 (March 18, 1988) and Mulhern, M., Everett, D.J., Perry, C.J., Hudson, P., Finn, J.P.; Report #: 7115 (March 21, 1989)). Troysan Polyphase P-100 (97% pure) was fed in diet to Sprague-Dawley rats (65/sex/dose) at 0, 20, 40 and 80 mg/kg/day for 104 weeks. At week 52, 15/sex/dose were necropsied (Report 5261) to assess chronic toxicity. At 104 weeks, 50/sex/dose were necropsied (Report 7115) to assess carcinogenicity. Chronic NOEL = 20 mg/kg/day (Group mean bodyweights for both the chronic and carcinogenicity studies were decreased at ≥ 40 mg/kg. Males at 80 mg/kg had hemoglobin, RBC counts and hematocrit that were statistically significantly decreased and at ≥ 40 mg/kg (chronic study) MCHC was decreased. Liver weights were increased at 52 weeks for both sexes at 80 mg/kg. Effects to the stomach were the primary macropathology effects observed at both 52 weeks (80 mg/kg) for chronic toxicity and at 104 weeks (≥ 40 mg/kg) for carcinogenicity. Histopathological effects were observed primarily in the stomach for both sexes at ≥ 40 mg/kg at 52 weeks and at 104 weeks and the incidence of effects had increased compared to 52 weeks. Salivary gland effects were observed in both sexes at ≥ 40 mg/kg (52 & 104 weeks).). No carcinogenicity. Possible adverse chronic effect: Treatment-related increase in stomach effect and effects to salivary glands at ≥ 40 mg/kg. M. Silva, 8/22/02.

EPA NOEL < 20 mg/kg (Decreased male body weight gain.) Core minimum.

CHRONIC TOXICITY, RAT

Subchronic study:

50237 011 045437 "90-Day Subchronic Oral Toxicity Test in Rats. Test Material Troysan Polyphase," (Gordon, E.B., Yuster, J.; Bioassay Systems Corporation, Woburn, MA; BSC #: 11787; 5/11/84). Troysan Polyphase (98% pure) was administered by gavage to Sprague-Dawley rats (10/sex/dose) at 0 (corn oil), 20, 50 and 125 mg/kg, 5 days/week for 13 weeks. A satellite group received 125 mg/kg (10/sex, 5 days/week) for 13 weeks, then were held without treatment for 28 days after the 13 week treatment. NOEL = 20 mg/kg (Absolute and relative body weights were decreased in males at 125 mg/kg. Clinical signs (excess salivation, lethargic, wheezing, epistaxis) in males at ≥ 50 mg/kg and in females at 125 mg/kg. Both sexes at 125 mg/kg had increased chronic progressive nephrosis of kidney, liver cytomegaly (all animals at 125 mg/kg), forestomach irritation and cardiomyopathy.) This study is not acceptable. It is possibly upgradeable upon submission of clinical sign data (mentioned but not included), inclusion of all data mentioned in the results section in summary tables with statistical analysis. Possible adverse effects indicated (clinical signs, liver hyperplasia, cardiomyopathy) M. Silva, 8/2/02

EPA NOEL = 20 mg/kg (Increased liver weights.) Not acceptable to EPA.

008 037437 Duplicate of 011 045437

016 064012 Duplicate of 011 045437.

**** 028 114798** "91-Day Dermal Toxicity Study in Rats With Troysan Polyphase P-100," (Siglin, J.C.; Springborn Laboratories, Inc., Life Sciences Division, Spencerville, OH; SLS Study #: 3228.14; 12/6/91). Troysan Polyphase P-100 (97.5% pure) was dermally administered to Sprague-Dawley Crl:CD_BR VAF/Plus_ rats (10/sex/dose) at 0 (PEG 400 = vehicle), 50, 200 and 500 mg/kg/day (with occlusion) for 91 days (6 hours/day, 5 days/week). Systemic NOEL = 50 mg/kg (Male body weight gains were statistically significantly decreased ($p < 0.05$) at 500 mg/kg early in the study but thereafter weight gains were similar to controls. Cumulative body weight gains for males were statistically significantly decreased ($p < 0.05$) over days 1 – 29 at 500 mg/kg, but thereafter weights were similar to controls. For males, food consumption was intermittently statistically significantly decreased at ≥ 200 mg/kg. Dermal NOEL = 50 mg/kg (Clinical effects (erythema, edema, eschar, desquamation) and histopathology (acanthosis, exudate, hyperkeratosis, ulcer) on skin were observed at ≥ 200 mg/kg.)) Possible adverse effect to skin. Acceptable. Silva, 8/23/02

EPA NOEL = 200 mg/kg. Core minimum.

CHRONIC TOXICITY, DOG

No study on file.

ONCOGENICITY, RAT

See COMBINED RAT

ONCOGENICITY, MOUSE

Dose-Range-finding Study:

50237 - 121 203593 "Iodopropynylbutyl Carbamate (IPBC) 2 Week Dose Range Finding Study in Mice," (Atkinson, C., Perry, C.J.; Inveresk Research International, Musselburgh, Scotland; IRI Project ID#: 436139; Report #: 3960; 8/14/87). Troysan Polyphase P 100 (3-iodo-2-propynyl butyl carbamate (IPBC), Batch P-2848-8603-P100; 97% pure) was fed in diet to CD-1 mice (5/sex/dose) at 0, 20, 80, 200, 500 and 1000 mg/kg/day for 2 weeks. NOEL = 200 mg/kg (Mild piloerection occurred in males at ≥ 500 mg/kg and in females at 1000 mg/kg. Body weights and food consumption were decreased at ≥ 500 mg/kg in both sexes. Both sexes at ≥ 500 mg/kg had increased absolute liver weights and females at ≥ 500 mg/kg had statistically significantly decreased absolute heart weights.) No adverse effects indicated. Data are supplemental. (Silva 9/24/03)

50237 - 0149 210211 "8-Week Dietary Dose Range Finding Study in Mice," (Atkinson, C., Perry, C.J., Aitken, R.; Inveresk Research International, Musselburgh, Scotland; IRI Project #: 436144; Report #: 5021; 10/26/87). Troysan Polyphase P 100 (3-iodo-2-propynyl butyl carbamate (IPBC), Batch P-2848-8603-P100; 97% pure) was fed in diet to CD-1 mice (10/sex/dose) at 0, 50, 250, 500 and 1000 mg/kg/day for 8 weeks. Systemic (chronic) NOEL = 50 mg/kg/day (At ≥ 250 mg/kg/day (M) and at

1000 mg/kg/day (F) there were decreased body weights. Food consumption was decreased in both sexes at ≥ 500 mg/kg/day. In males there was a decrease in absolute heart (≥ 250 mg/kg/day), kidney (≥ 500 mg/kg/day) and spleen (1000 mg/kg/day) weights and an increase in absolute liver weights (≥ 250 mg/kg/day). Males showed an increase in relative liver weights at ≥ 250 mg/kg/day. In females there was a decrease in absolute heart, kidney and lung weights at 1000 mg/kg/day and an increase in absolute liver weights at 1000 mg/kg/day. Females showed increased relative liver weights at ≥ 250 mg/kg/day. At 500 mg/kg/day (M: 2/10) and 1000 mg/kg/day (M: 6/10) and at 1000 mg/kg/day (F: 2/10) had darkened liver. There was increased centrilobular enlargement at ≥ 250 mg/kg/day (M) and at ≥ 500 mg/kg/day (F). There was an increase in centrilobular brown pigmentation at ≥ 250 mg/kg/day (M) and at ≥ 500 mg/kg/day (F). In both sexes at ≥ 500 mg/kg/day there was an increase in Kupffer-cell brown pigmentation. There was an increase in brown-pigmented concretion in bile and in portal tract inflammation in livers of both sexes at 1000 mg/kg/day. There was also a slight increase in single cell necrosis at ≥ 250 mg/kg/day and in focal necrosis at 1000 mg/kg/day in livers of males. The report noted that there was a dose-related redistribution of intracellular lipid that was more evident at doses below 500 mg/kg/day. It was stated that the changes at the higher doses might have been masked by the other hepatocyte changes occurring at the same time. The amount of intracellular lipid was decreased in the treated animals, and the effects were most evident in the hypertrophied hepatocytes.) Possible adverse effect indicated (hepatotoxicity). M. Silva, 11/15/04

50237 - 031 114802 Summary of 50237 - 0149 210211, reviewed above.

Definitive Study:

** 50237 – 031 114803 "IPBC 78 Week Dietary Carcinogenicity Study in Mice", (Mulhern, M., Finn, J.P., Everett, D.J., Perry, C.J.; Inveresk Research International, Tranent, Scotland, Report # 7304, 6/16/89). Troysan Polyphase P 100 (3-iodo-2-propynyl butyl carbamate (IPBC), Batch P-2848-8603-P100; 97% pure) was fed in diet to CD-1 mice (50/sex/dose) at 0, 20, 50 and 150 mg/kg/day for 78 weeks. Plasma, RBC and Brain ChE were not inhibited. Systemic (chronic) NOEL < 20 mg/kg/day (Group mean bodyweights were slightly reduced for males (3-8%) and females (3-6%) at 150 mg/kg. Bodyweight gain was 23% (M) and 20% (F) lower at 150 mg/kg through week 78, compared to controls. Thyroids were enlarged macroscopically at 150 mg/kg in both sexes (especially males). There were histopathological thyroid effects in both sexes at all doses.) There was a statistically significant increase in hepatocytic adenomas at 150 mg/kg in males but not in females. The incidence of liver carcinomas in males was similar in all groups (3, 3, 3, 4 for control through high dose). Originally reviewed as unacceptable but possibly upgradeable (Silva, 8/27/02) upon review of the requested information, the study has been upgraded to acceptable. Results of the Pathology Working Group (PWG, see 50237-122/203594) re-evaluation of liver histopathology showed that there was not a treatment-related association for hepatocellular adenomas and carcinomas. Based on the results of the PWG, the study is no longer flagged for adverse oncogenic effects. (Silva, 11/29/04)

EPA NOEL < 20 mg/kg (Thyroid effects).

50237 - 031, 122 114803, 203594 "Pathology Working Group (PWG) Report on the 78-Week Dietary Carcinogenicity Study of 3-Iodo-2-Propynyl Butyl Carbamate (IPBC) in CD01 Mice," (Goodman, D.G.; Pathco, Inc., Ijamsville, MD; 2/2/95). This volume contains the results of an independent panel review of the livers from the 78-week oncogenicity study of IPBC in CD-1 mice. Hematoxylin and eosin-stained microscopic slides (both sexes), individual animal data and study results were submitted to the independent consulting company PATHCO, Inc. (PWG) for evaluation of liver pathology. An independent evaluation by independent consultant R.A. Squires (Peer Review Pathologist) and by 4

veterinary pathologists who were contracted by PATHCO, Inc (PWG) were submitted. PWG results showed in females there was no increase in the incidence of hepatocellular tumors or foci of cellular alterations. Males had statistically significantly increased hepatocellular adenomas at 150 mg/kg ($p < 0.05$; also observed in the original report), a positive trend test for hepatocellular adenomas ($p < 0.05$) with no increase in hepatocellular carcinomas or foci. This is similar to what was described by Squires. Upon re-evaluation of the data, the historical controls and the rebuttal document, the adverse effect flag on this report has been removed. (Silva, 11/24/04)

REPRODUCTION, RAT

032 114804 "Two Generation Oral (Dietary Administration) Reproduction Toxicity Study in the Rat (One Litter per Generation)", (Osterburg, I.; Reproduction Toxicology, Hazleton Laboratories Deutschland GmbH, Munster, West Germany; Report # 548-511/3, 10/16/87). Troysan Polyphase (3-iodo-2-propynyl butyl carbamate (IPBC), Batch #: 2710-8511-R100, purity not stated) was fed in diet to Sprague Dawley Crl:CD- (SD) BR rats (25/sex/dose/generation) at 0, 120, 300 and 750 ppm for 2 generations (1 litter/generation) through weaning of F2 pups. Exposure began 14 weeks prior to mating of F0 parental animals. Parental NOEL = 120 ppm (During premating, both P and F1 parental food consumption was reduced intermittently in both sexes at 750 ppm. Body weight during premating was slightly decreased at ≥ 300 ppm in males. During gestation, P females had decreased body weight gain at 300 ppm but not at 750 ppm. Throughout premating, F1 parental males had decreased body weight and body weight gain at 750 ppm.) Reproductive NOEL = 300 ppm (Both F1 and F2 litter size and litter weights were decreased at 750 ppm. The F1 pups had decreased live birth index at 750 ppm. F2 pups had decreased live birth index at 750 ppm. There were no effects on reproductive parameters.) This study is not acceptable, since characterization of Troysan Polyphase (purity, stability, content) and analyses of dosing material (homogeneity, stability, concentration) were not included in the study. It is necessary to submit these data for a possible upgrade of this study to acceptable. No adverse effect. Green & Silva, 9/3/02.

EPA Parental NOEL = 300 ppm (Based on decreased parental body weights and food consumption. Reproduction NOEL ≥ 750 ppm.

008 037438 "Preliminary Study for a 2 Generation Study in the Rat," (No author indicated; Hazleton Laboratories Deutschland GmbH; Project #: 511/1; no date). Troysan Polyphase (no characterization) was administered by gavage to 16 inseminated rats at 80 mg/kg. Data could not be interpreted, since there were no controls. Although most of the report was in German, there did not appear to be any treatment-related effects. (No worksheet). M. Silva.

TERATOLOGY, RAT

027 114797 "Final Report, Troysan Polyphase Oral (Gavage) Teratogenicity Study in the Rat," (Osterburg, I., Hazleton Laboratories Deutschland GmbH, Munster, West Germany, Report # 696-511/4, 12/86). Troysan Polyphase P100 (purity not stated) was administered by gavage to mated Sprague Dawley Crl:CD(SD)BR rats (28 – 38/dose) at 0 (corn oil), 20, 50 or 125 mg/kg/day on gestation days 6 through 15. Maternal NOEL = 20 mg/kg/day (Bodyweight gain was decreased and total litter resorptions was increased at ≥ 50 mg/kg.). Possible adverse effects indicated: Developmental NOEL = 20 mg/kg/day (Fetal malformations (cleft palate, bilateral anophthalmia) at 50 mg/kg and skeletal (scholiosis)

and external malformations (mandible shortened, open eye) at 125 mg/kg were observed.). Not acceptable and probably not upgradeable (No dose justification, historical control data for total litter resorptions and fetal malformations, food consumption measurements, test article/dosing material characterization). At this time, the adverse fetal effects are considered to be treatment-related. Adverse fetal effects occurred at doses causing only mild maternal toxicity (transitional decreased body weight gain). (Green & Silva, 7/31/02).

EPA Maternal NOEL = 50 mg/kg (Decreased weight gain in dams.) Developmental NOEL = 50 mg/kg (Based on delayed ossification in fetuses.)

016 064015 Duplicate of 027 114797.

TERATOLOGY, RABBIT

Range-finding Study:

035 117971, "Range-Finding Teratology Study in Rabbits with Troysan Polyphase P-100," (Siglin, J.C.; Springborn Laboratories, Inc. (SLS), Life Sciences Division, Spencerville, OH., Report # 3228.15; 8/17/92). Troysan Polyphase P-100 (97% 3-iodo-2-propynyl butyl carbamate) was administered by gavage to inseminated New Zealand White female rabbits (5/dose) at 0 (corn oil), 5, 15, 30, 50 and 80 mg/kg/day on gestation days 6 through 18. Maternal NOEL = 30 mg/kg/day (At 50 mg/kg, an increase in post-implantation loss and a decrease in mean number of viable fetuses was observed. Gross necropsy findings for 2/4 females found dead at 80 mg/kg showed gastrointestinal changes. However, tissue autolysis occurred to the point where gross necropsy could not be performed on the other 2/4 females at 80 mg/kg that had died on study. At 80 mg/kg females showed unkempt appearance, decreased activity, emaciation, dehydration, few feces, no feces and desquamation around the mouth. At 80 mg/kg bodyweight continued to decrease.) Developmental NOEL = 30 mg/kg/day (External malformations occurred in 2/21 fetuses at 50 mg/kg (exencephaly, flexed paw) from 2 different litters). No adverse effects indicated. Data are supplemental. (H. Green & M. Silva, 3/8/02)

Definitive Study:

** 035 117972 "Teratology Study in Rabbits with Troysan Polyphase P-100," (Siglin, J.C.; Springborn Laboratories, Inc. (SLS), Life Sciences Division, 553 North Broadway, Spencerville, OH., Report # 3228.16; 8/17/92). Artificially inseminated New Zealand White female rabbits received Troysan Polyphase P-100 (97% 3-iodo-2-propynyl butyl carbamate) at 0 (corn oil), 2, 20, and 50 mg/kg/day by gavage on gestation days 6 through 18. Maternal NOEL = 20 mg/kg/day (2 females died and 1 was sacrificed moribund at 50 mg/kg/day. There was an increase in post-implantation loss and decrease in mean number of viable fetuses at 50 mg/kg. The number of live litters and the mean live litter size was reduced at 50 mg/kg/day. There was an increased incidence in few feces, no feces, soft stools, mucoid stools, brownish colored mucoid material in cage/tray, reddish colored material in cage/tray, fecal stain, various nose/mouth effects in dams at 50 mg/kg. Maternal food consumption at 50 mg/kg was reduced (18% to 40%) throughout treatment period. Group mean bodyweights were decreased by nearly 10% (day 19). There were statistically significantly decreased body weight gain throughout the study at 50 mg/kg.) **Developmental NOEL** = 20 mg/kg/day (There were increased fetal soft tissue and skeletal malformations at 50 mg/kg. There was an increased incidence in flexed paw, heart/great vessel anomaly,

hydrocephaly and hyoid body/arch unossified at 50 mg/kg.) Acceptable. No adverse effect. (M. Silva & H. Green, 3/12/02).

EPA Developmental NOEL = 20 mg/kg; Developmental NOEL \geq 50 mg/kg.

GENE MUTATION

010 045436, "Salmonella Typhimurium/Mammalian Microsome Plate Incorporation Assay with Compound IPBC", (N.E. McCarroll, Hazleton Laboratories America, Inc., Vienna, VA., Report # 2277-102, 7/24/84). Triplicate plates of *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538 were exposed in the presence and absence of activation (S9) to 3-iodo-2-propynyl butyl carbamate (IPBC) concentrations of 0 (untreated), 0 (DMSO), 0 (S9 fraction), 6.2, 18.5, 55.6, 166.7 and 500.0 μ g/plate for 48 hours. A treatment-related increase in gene mutations was not observed. The positive controls functioned as expected. Currently this study is not acceptable but is possibly upgradeable with submission of the requested information (chemical characterization, dosing solution analyses/data for toxicity tests, individual plate counts). Green & Silva, 8/1/02

008 037441 Duplicate of 010 045436

016 064014 Duplicate of 010 045436

** 026 114794, "Testing for Mutagenic Activity with Salmonella typhimurium TA 1535, TA 1537, TA 1538, TA 98, and TA 100," (C. G. Riach, Inveresk Research International Limited, Musselburgh, Scotland, Report # 4896, 6/20/89). *Salmonella typhimurium* strains TA98, TA100, TA1535, TA1537, and TA1538 were treated for 48 hours (3 plates/dose; with and without S9 metabolic activation) with Troysan Polyphase P-100 (98.68% 3-iodo-2-propynyl butyl carbamate) at 0 (DMSO), 1, 3, 10, 33, 100 and 333 μ g/plate (Test #1, +/- S9) or 0, 3, 10, 33, 100, 333 and 1000 μ g/plate (Test #2, + S9) or 1, 3, 10, 33, 100 and 333 μ g/plate (Test #2, no S9) and TA1535 treatment ranged from 3 to 1000 μ g/plate. An increased incidence in reverse mutations was not observed. Acceptable. (Green & Silva, 6/27/02).

CHROMOSOME EFFECTS

** 026 114796, "Troysan Polyphase (IPBC): In Vivo Micronucleus Assay in Mice, Final Report," (N. McCarroll, Hazleton Biotechnologies Corporation, Vienna, VA., Report # 2277-103, 10/3/84). 3-Iodo-2-propynyl butyl carbamate (IPBC, 99% purity) was administered in a single dose by gavage to CD-1 mice (15/sex/dose) at 0 (corn oil), 200, 660, and 2000 mg/kg. At 30, 48, and 72 hours after dosing, bone marrow was sampled (5/sex/dose). No increase in the frequency of micronucleated polychromatic erythrocytes was observed. Acceptable with no adverse effect. (Green & Silva, 7/29/02).

008 037440 Duplicate of 026 114796

016 064013 Duplicate of 026 114796

DNA DAMAGE

026 114795 "Troysan Polyphase (IPBC): Assessment of Genotoxicity in an Unscheduled DNA Synthesis Assay Using Adult Rat Hepatocyte Primary Cultures," (D. McBride and C.G. Riach, Inveresk Research International, Musselburgh EH21 7UB Scotland, Report # IRI 737447, 1/21/88). Primary hepatocyte cell cultures obtained from Fischer 344 rats were treated (4 plates/dose) with IPBC (3-iodo-2-propynyl butyl carbamate) at 0 (DMSO), 3.0, 4.5, 6.0, 7.5, 9.0, 10.5, 12.0, and 13.5 µg/ml for 18 to 20 hours in a test for unscheduled DNA synthesis. Unscheduled DNA synthesis was not observed. Unacceptable and upgradeable (test article characterization, statistical analyses and clarification of grouping for individual data). (Green & Silva, 7/25/02).

NEUROTOXICITY

** 50237 – 137 & 0151 207093, 211914 "Acute Oral Neurotoxicity Study with 3-Iodo-2-Propynyl Butyl Carbamate (IPBC) Administered by Gavage in CD[®] Rats," (Weiler, M.S.; Covance Laboratories, Inc., Madison, WI; Laboratory Study ID#: Covance 7071-101; 8/31/01). IPBC (3-iodo-2-propynyl butyl carbamate; 99.3 - 101% pure) was administered by gavage in a single dose to Crl:CD[®](SD)IGS BR rats at 0 (corn oil), 100, 300 and 1000 mg/kg. Three sets of animals were treated as follows: Set 1: Functional Observation Battery (FOB)/Motor Activity (MA) and blood ChE pretest and at Time of peak effect day 1, including Brain ChE (12 rats/sex/dose). Set 2: FOB/MA, blood ChE pretest and at Time of Peak Effect on day 1 (3 to 6 hours after dosing) and on days 8 and 15. Brain ChE day 15 (12/sex/dose). Set 3: Six/sex/dose necropsied day 15 for neurohistopathology following *in situ* perfusion. Systemic NOEL < 100 mg/kg (There were numerous clinical effects observed in both sexes of Set 2 animals at 1000 mg/kg (hunched, hypoactive, liquid feces, few feces, periorbital squinting in eyes, effects on skin, and behavioral effects). There was a statistically significant decrease in motor activity in both sexes of Set 1 and 2 animals at ≥ 100 mg/kg on day 1. In Set 2 males (day 15), there was a statistically significant decrease in motor activity at ≥ 100 mg/kg. There was a statistically significant decrease in body weight gain in both sexes (Set 2) at ≥ 300 mg/kg days 1 - 8, in both sexes at 1000 mg/kg throughout the study. Set 3 males at ≥ 300 mg/kg had statistically significantly decreased body weight gain days 1-8 and 1-15. There was a statistically significant decrease in plasma ChE at ≥ 300 mg/kg (day 8) and at 1000 mg/kg (day 15) in Set 2 females.) Neurotoxicity NOEL = 300 mg/kg (Locomotor activity, Sets 1 & 2 on day 1 was statistically significantly decreased in both sexes at 1000 mg/kg. There was a statistically significantly decreased approach response in males at 1000 mg/kg (Sets 1 & 2). In Set 2 on day 8, there was a decrease in approach response in females at 1000 mg/kg. Females in Sets 1 & 2 had a statistically significant decrease in number of rears on day 1 at 1000 mg/kg.) Previously reviewed as unacceptable (Silva, 10/21/03), upon submission of a positive control (DPR volume/record #: 50237 – 0151/211914) the study is upgraded to acceptable. No adverse effect. Silva, 11/16/04.

** 50237 – 138 & 0151 207095 & 211915 "13-Week Neurotoxicity Study with 3-Iodo-2-Propynyl Butyl Carbamate (IPBC) in CD[®] Rats," (Weiler, M.S.; Covance Laboratories, Inc., Madison, WI; Laboratory Study ID#: Covance 7071-103; 9/20/01). IPBC (3-iodo-2-propynyl butyl carbamate; 99.3% pure) was fed in diet to Crl:CD[®](SD)IGS BR rats at 0, 10, 50 and 120 mg/kg for 4, 8 and 13 weeks. A recovery group was held until 17 weeks (4 week recovery) before sacrifice. Four sets of animals were treated as follows: Set 1: Functional Observation Battery (FOB)/Motor Activity (MA) and blood ChE pretest, weeks 4, 8, 13; Brain ChE week 13 (12 rats/sex/dose). Set 2: FOB/MA, blood ChE and Brain ChE week 17 (12/sex at 0 & 120 mg/kg). Set 3: Six/sex/dose necropsied week 13 for

neurohistopathology; 6/sex/dose necropsied at week 17. Set 4: 12/sex/dose brain ChE week 4; 12/sex/dose brain ChE week 8. Systemic NOEL = 10 mg/kg (Both sexes in all sets had statistically significantly decreased mean body weights at 120 mg/kg (also decreased throughout recovery in males, but not females). Both sexes had statistically significant decreases in food consumption at ≥ 50 mg/kg.) Neurotoxicity NOEL = 50 mg/kg (There were minimal effects in both sexes in the FOB at 120 mg/kg.) There was no clear treatment-related neurohistopathology. Previously reviewed as unacceptable (Silva, 10/21/03) upon receipt of the requested data, this study is now acceptable with no adverse effect. Silva, 11/15/04

50237 – 0151 211914 “Acute Neurotoxicity Validation Study with Paraoxon in Rats,” (Weiler, M.S., Hazleton Wisconsin, Inc., Madison, WI; Laboratory Project Identification #: HWI 2100-004; 4/11/96). This is a positive control study for the definitive acute neurotoxicity study.

50237 – 0151 211915 “Neurotoxicity Validation Study with Acrylamide in Rats,” (Weiler, M.S., Hazleton Wisconsin, Inc., Madison, WI; Laboratory Project Identification #: HWI 2100-030; 3/29/96). This is the positive control for the definitive subchronic neurotoxicity study.

The following record numbers have been reviewed:

<u>Record Number</u>	<u>Volume</u>
037438	50237-008
037440	50237-008 (Duplicate to 114796).
037441	50237-008 (Duplicate to 045436).
045435	50237-010 (Duplicate to 114796).
045436	50237-010
064013	50237-016 (Duplicate to 114796).
064014	50237-016 (Duplicate to 045436).
064015	50237-016 (Duplicate to 114797).
114794	50237-026
114795	50237-026
114796	50237-026
114797	50237-027
114800	50237-029
114801	50237-030
114803	50237-031
114805	50237-032
114804	50237-032
117971	50237-035
117972	50237-035
